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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,289	05/31/2002	Vega Masignani	PP01639.102; 2300-1639	6882

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Chiron Corporation
Intellectual Property Department R440
PO Box 8097
Emeryville, CA 94662-8097

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/031,289	**Applicant(s)** MASIGNANI ET AL.	
	Examiner S. Devi, Ph.D.	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 December 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *three* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Attachment.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1,10 and 25-32*.
   Claim(s) withdrawn from consideration: *7,9,13,15,17,19,21,23 and 24*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☒ Other: Attachment.

S. Devi 12/6/05

S. DEVI, PH.D.
PRIMARY EXAMINER

ATTACHMENT TO ADVISORY ACTION

Applicants' After-final Amendment

1) Acknowledgment is made of Applicants' after-final amendment filed 12/05/05 in response to the final Office Action mailed 10/04/05.

Status of Claims

2) Claim 1 has been amended via the amendment filed 12/05/05.

Claims 1, 7, 9, 10, 13, 15, 17, 19, 21 and 23-33 are pending.

Claims 1, 10 and 25-32 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

5) The rejection of claim 1 made in paragraph 17(a) of the Office Action mailed 10/04/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

6) The rejection of claims 10 and 25-32 made in paragraph 17(b) of the Office Action mailed 10/04/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

Rejection(s) Maintained

7) The rejection of claim 1 and those dependent therefrom made in paragraph 15 of the Office Action mailed 10/04/05 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is maintained for reasons set forth therein and herebelow.

Applicants submit the following arguments: (a) Lines 7-9 of page 2 of the specification indicate that the invention includes polypeptides that have 70% sequence identity to the protein

fragments. (b) Lines 18-22 of page 2 of the specification states that 'The proteins of the invention can, of course be prepared by various means (e.g., recombinant expression, purification from cell culture, chemical synthesis, etc.) ...'. One of skill in the art would readily recognize that purification from cell culture would result in a purified polypeptide as is presently claimed. (c) The specification conveys to one of skill in the art that the inventors had possession of 'a purified polypeptide comprising a contiguous amino sequence with at least 70% sequence identity to the sequence of SEQ ID NO: 133'. (d) Lines 20-27 on page 3 of the specification indicate that the invention 'also provides the use of nucleic acid, protein, or antibody according to the invention [e.g., such as the claimed purified polypeptides] in the manufacture of: ..... (iii) a reagent which can raise antibodies against Neisserial bacteria'. One of skill in the art would readily recognize that a polypeptide that may be used as a reagent which can raise antibodies against Neisserial bacteria would have 'at least one antigenic determinant that elicits an immune response against Neisserial bacteria' as is presently claimed.

Applicants' arguments have been carefully considered, but are not persuasive. Lines 7-9 of page 2 of the specification do not describe a 'purified' polypeptide comprising a contiguous amino acid sequence with at least '70%' sequence identity to 'the sequence of' SEQ ID NO: 1331, wherein the polypeptide ..... elicits an immune response against Neisserial bacteria' and has a length of 100 amino acids or less. Lines 7-9 of page 2 of the specification describe homolgs (i.e., mutants and variants) having sequence identity to polypeptide fragments. Lines 20-27 on page 3 of the specification do not describe the claimed 'purified' polypeptide comprising a contiguous amino acid sequence with at least '70%' sequence identity to 'the sequence of' SEQ ID NO: 1331 (i.e., a mutant and variant of the polypeptide fragment), wherein the polypeptide mutant or variant having the recited percent identity serves as a reagent that can 'raise antibodies against Neisserial bacteria'. Lines 20-27 on page 3 of the specification instead describe a 'protein' that can be used as a reagent which can raise antibodies against neisserial bacteria. The specification, as originally filed, is not supportive of a purified polypeptide having 70% sequence identity to the amino acid sequence of SEQ ID NO: 1331 (i.e., a mutant or variant of the polypeptide fragment) and concurrently having an antigenic determinant that has the ability to 'elicit an immune response against' the generically recited 'Neisserial bacteria'. The specification, as originally filed, does not attach any function to the at least 70% identical variant or mutant of the polypeptide fragment. An at least 70% identical variant of the

polypeptide fragment of SEQ ID NO: 1331 having at least one antigenic determinant of neisserial bacteria as recited and that is *purified from cell culture* lacks descriptive support in the instant specification. The rejection stands.

8) The rejection of claims 1, 10 and 25-32 made in paragraph 16 of the Office Action mailed 10/04/05 under 35 U.S.C. § 112, first paragraph, as being non-enabled with regard to the scope, maintained for reasons set forth therein and herebelow.

Applicants submit the following arguments: (a) Lines 8-29 on page 37 and page 64-71 of the specification disclose preferred fragments 114-1 (SEQ ID NO: 1331). (b) The Office appears to be asserting that in order for an invention to be enabled, one of skill in the art must be able to predict with 100% accuracy whether any given polypeptide meeting the sequence identity would provide the claimed function. However, by analogy to monoclonal antibodies, this is not required for enablement. It is well established that claims to monoclonal antibodies directed to a particular protein are enabled where the application discloses the sequence of the protein. With just the protein sequence, one of skill in the art could not predict the sequences of any of the monoclonal antibodies directed to that sequence. However, such claims are enabled because it is a routine procedure to immunize an animal such as a rabbit with the protein, generate monoclonal hybridoma from the rabbit, and screen them for monoclonal antibodies which are directed to the protein. (c) With the present claims, the procedure is very similar and even more routine. One of skill in the art need only synthesize a set of peptide fragments of the claimed sequence identity and length limitations, the selection of which may be guided by the preferred fragments listed in the specification. Such synthesis was so routine as of the priority date of the present application that one of skill in the art could order such purified polypeptides from a company. Then the person of ordinary skill in the art need merely immunize an animal such as a rabbit and drawn and screen blood for polyclonal antibodies which recognize the original protein 114-1 (i.e., a Neisserial bacterial protein). Drawing and screening polyclonal antibodies in the blood is an even simpler task than generating hybridoma and screening monoclonal antibodies produced from them. This addresses the Office's concerns regarding any unpredictability and the amount of experimentation required.

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' assertion, monoclonal antibodies directed to an enabled protein of known structure and the alleged lack of undue experimentation in the production of such monoclonal antibodies are not

analogous to the instantly claimed at least 70% identical variants of a polypeptide fragment comprising the 18 amino acid-long SEQ ID NO: 1331. In the instant case, the claims are not drawn to monoclonal antibodies to a given protein. The instant application does not disclose the precise structure of a purified polypeptide variant having 70% sequence identity to the amino acid sequence of SEQ ID NO: 1331 *and* concurrently having an antigenic determinant that has the ability to 'elicit an immune response against' the generically recited 'Neisserial bacteria'. Lines 8-29 on page 37 and page 64-71 of the specification disclose the fragment 1331 of ORF114-1 from WO 99/36544. This fragment 1331 of ORF114-1 as recited in Table I at page 67 of the specification is **not** a 70% identical variant of the polypeptide having the amino acid sequence of SEQ ID NO: 1331. Instead, it is the fragment 1331 corresponding to SEQ ID NO: 1331. The instant rejection does not apply to a 'purified polypeptide comprising the amino acid sequence of SEQ ID NO: 1331, .. wherein the polypeptide comprises at least one antigenic determinant that elicits an immune response against neisserial bacteria and has a length of 100 amino acids or less', but to at least 70% identical variants thereof. Even if a skilled artisan made a series of variants of SEQ ID NO: 1331, there is absolutely no predictability that the resulting variants having as much as 30% non-identity to SEQ ID NO: 1331 would have the recited function, i.e., would remain *Neisseria*-specific. For these reasons and the those, including the functional unpredictability of polypeptide variants and undue experimentation, fully established at paragraphs 14 and 16 of the Office Action mailed 10/04/05, the rejection stands.

Remarks

9) Claims 1, 10 and 25-32 stand rejected.

10) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses and papers is (571) 273-8300.

11) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

December, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER